

**REMARKS**

***Status of the Claims***

The Office Action dated October 1, 2004 presents the examination of claims 25-26, 43, 45-46, 49, 57, 59-61, and 66-68. Claims 25 and 26 are allowed. Claims 59 and 66 are canceled without prejudice or disclaimer of the subject matter recited therein. Claims 43, 45, and 57 are amended to clarify claim language. Support for subject matter added to claim 43 is found on page 55 of the specification, and support for subject matter added to claim 57 is found on page 55 of the specification and in former claims 59 and 66. No new matter is inserted into the application. Upon entry of this Reply, claims 25-26, 43, 45-46, 49, 57, 60-61, and 67-68 will be pending.

***Amendments to the Specification***

Pages 50 and 55 of the specification are amended. Specifically, minor typographical errors in the VTT numbers of strains E-991203 and E-991204 are corrected on page 50. Support for the correct VTT numbers is found elsewhere in the specification, such as on page 55, lines 24 and 25.

Further, the Accession numbers for strains VTT E-991203 and VTT E-991204 are added to page 55. Support for the Accession numbers is found in the Receipt of Original Deposit for VTT E-991203 and VTT E-991204 issued by the DSMZ-Deutsche Sammlung von

Mikroorganismen und Zellkulturen GmbH International Depository Authority. A copy of each Receipt is attached hereto.

Applicants note that the addition of information designating the depository, accession number, and deposit date of deposited biological material to the specification may be added after the filing date, and is not considered new matter. See, In re Lundak, 773 F.2d 1216 (Fed. Cir. 1985); U.S. Pat. & Trademark Off., *Manual Pat. Examining Proc.* § 2406.01 (8<sup>th</sup> ed., Rev. 2 2004). Therefore, no new matter is inserted into the application.

#### **Interview**

An Interview was held with the Examiner and Supervisory Examiner at the United States Patent and Trademark Office on January 11, 2005. The assistance of the Examiner and Supervisory Examiner in advancing prosecution of the present application is greatly appreciated. In the Interview Summary, the Examiner writes,

The Applicant agreed to correct the elements of claims 43 and 57 that are subject of objections and rejection under 35 USC 112, second paragraph. The examiner emphasized the extremely large scope of claims 43 and 57 makes the claims unsearchable. The Applicants discerned three issues in the claims limitations: polynucleotides, microorganisms and products. The claims as amended limit products only. The examiner

stressed the necessity of recitation in the claims of particular genes encoding enzymes to be used for increasing yield of product. The recitation which would allow searching for prior art. The applicant will consider the examiner's suggestion. The examiner continues to emphasize the application contains allowable subject matter which comprises particular transformants of *S. cerevisiae*, *S. pombe* and *Corynebacterium*, and the method of their use for production of particular products, as disclosed.

During the interview, the Supervisory Examiner stated that it was difficult to understand the claims. In particular, the Supervisory Examiner inquired as to whether an additional gene, other than the polynucleotides recited in the claims, is necessary to perform the methods of claims 43 and 57. Furthermore, the Supervisory Examiner inquired as to whether the second paragraph of claim 43 limits the scope of the claim in any way. In this regard, the Supervisory Examiner stated that depletion or increase of co-factors is an inherent characteristic of any enzyme acting in a catalytic manner. The Supervisory Examiner suggested amending claims 43 and 57 to more fully describe the claimed method.

Taking into consideration the Supervisory Examiner's remarks, Applicants present herein amendments to claims 43 and 57. Most of these amendments are non-narrowing in nature and serve to clarify the claim language. In claim 43, for example,

the steps of the method are more succinctly set forth, and a final clause is added comparing the final product of the transformed microorganism versus a microorganism which has not been transformed with any of the polynucleotides recited in the claim. Applicants respectfully submit that all steps necessary for performing the invention are presented in the claims.

Applicants have also deleted the second paragraph of claim 43. With regard to the Supervisory Examiner's statement that any enzyme depletes or increases cofactors, Applicants agree that enzymes that have cofactors (most do not) deplete or increase the amount of those cofactors when they catalyze reactions in vitro. However, in an organism, the changes in cofactor amounts caused by one enzyme are balanced by other enzymatic reactions such that a pseudo steady state is created, in which the levels of all cofactors are maintained at a constant amount.

This internal balancing, however, sometimes breaks down when microorganisms are used in certain industrial processes such that a net depletion in the amount of intracellular cofactors (i.e., NAD and NADPH) occurs. The present invention solves this problem by genetically engineering production microorganisms to improve their properties so that they produce useful products (i.e., ethanol, xylitol, lysine, etc.) more efficiently.

Based on the above, Applicants respectfully submit that the amended claims and remarks submitted herein fully clarify the present invention which is recited in the claims.

***Objections to the Claims***

The Examiner objects to claims 43 and 57 for minor informalities. Applicants respectfully traverse. Reconsideration and withdrawal of the instant objection are respectfully requested.

Specifically, the Examiner states that the term "molecules" is missing after the words "NADPH" and "NADP" in claim 43, and that the adverb "normally" is not necessary in claims 43 and 57. The words "NADPH" and "NADP" and that the adverb "normally" have been deleted from the claims.

These amendments to claims 43 and 57 are made to clarify and/or improve claim language and do not affect the scope of the claims in any way. Withdrawal of the instant objection is respectfully requested.

***Constructive Election***

The Examiner asserts that claims 43, 45, 46, 49, and 66 are directed to a non-elected invention, and constructively withdraws these claims from consideration. Applicants

respectfully traverse the constructive election and request withdrawal thereof.

The Examiner states that only methods for the production of ethanol are considered. Applicants respectfully submit that the products recited in claims 43 and 57 all relate to a single inventive concept under PCT Rule 13.1 in that industrial production of all of these products in a microorganism results in either a depletion of NAD/NADPH cofactors or an increase in NADH/NADP cofactors. Therefore, the claims of the present invention possess unity of invention under PCT rules.

For this reason, the Examiner is respectfully requested to withdraw the constructive election, and examine the entire scope of the claims.

***Rejection under 35 U.S.C. § 112, second paragraph***

The Examiner rejects claims 43 and 57 under 35 U.S.C. § 112, second paragraph for allegedly being indefinite. Applicants respectfully traverse. Reconsideration of the claims and withdrawal of the rejection are respectfully requested.

Specifically, the Examiner asserts that the recitation of "a microorganism" in the 6<sup>th</sup> and 9<sup>th</sup> lines of claims 43 and 57 is unclear. In order to clarify the claim language, the first recitation of "microorganism" is amended to "host

microorganism," and the second recitation of "microorganism" is amended to "transformed microorganism."

During the interview, the Examiner and Supervisory Examiner indicated that these amendments would overcome the rejection under 35 U.S.C. § 112, second paragraph. Withdrawal of the instant rejection is therefore respectfully requested.

***Rejection under 35 U.S.C. § 112, first paragraph***

***Polynucleotides***

The Examiner rejects claims 43, 45-46, 49, 57, 59-61, and 66-68<sup>1</sup> under 35 U.S.C. § 112, first paragraph for allegedly lacking adequate written description. Claims 59 and 66 are canceled, thus rendering rejection thereof moot. Applicants respectfully traverse the rejection applied to the pending claims. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

Specifically, the Examiner asserts that there is not adequate written description in the specification for the genus of "polynucleotides" and "microorganisms" recited in claims 43 and 57. Applicants respectfully disagree.

First, the genus of "polynucleotides" recited in claims 43 and 57 is limited to those encoding glutamate dehydrogenase,

malic enzyme, aldehyde dehydrogenase, malate dehydrogenase, glycerol-3-phosphate dehydrogenase, xylose-1-dehydrogenase, glyceraldehyde-3-phosphate dehydrogenase, orotate reductase, and ferredoxin reductase. These polynucleotides are well known in the art, and therefore are adequately described in the specification.

With regard to a genus of "microorganisms", the Examiner asserts that the specification only provides adequate written description for *S. cerevisiae* and *S. pombe*. However, during the interview, the Supervisory Examiner stated that she was satisfied with the recitation of "microorganism," so long as neither the inventive step nor the success of the method are dependent upon the type of microorganism used. Upon information and belief, Applicants confirm that the inventive step and the success of the inventive method are not dependent upon the type of microorganism used. However, in order to expedite prosecution of the present application, claims 43 and 57 are amended to recite that the microorganism is selected from the group consisting of yeast and *Corynebacteria*. Written description for yeast and *Corynebacteria* is found on page 55 of the specification and in the Examples.

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<sup>1</sup> The Examiner erroneously lists claim 48 as being rejected. Applicants respectfully note that claim 48 was canceled in the Reply filed on May 21, 2004. Correction of the record is therefore respectfully requested.

Applicants respectfully submit that pending claims fully satisfy the requirements of 35 U.S.C. § 112, first paragraph. Withdrawal of the instant rejection is therefore respectfully requested.

Products

The Examiner also rejects claims 57, 59, 60, 67, and 68 under 35 U.S.C. § 112, first paragraph for allegedly lacking written description. Claim 59 is canceled, thus rendering rejection thereof moot. Applicants respectfully traverse the rejection applied to the pending claims. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

Specifically, the Examiner asserts that there is not adequate written description in the specification for the genus of products produced by the method of claim 57. In order to overcome this rejection, Applicants insert the subject matter of non-rejected claim 66 into claim 57, and cancel claim 66. During the interview, both the Supervisory Examiner and Examiner agreed that this amendment would overcome the rejection for lack of written description.

Applicants respectfully submit that pending claims fully satisfy the requirements of 35 U.S.C. § 112, first paragraph.

Withdrawal of the instant rejection is therefore respectfully requested.

**Conclusion**

Applicants respectfully submit that the above remarks and/or amendments fully address and overcome the outstanding rejections and objections. For the foregoing reasons, Applicants respectfully request the Examiner to withdraw all of the outstanding rejections and objections, and to issue a Notice of Allowance indicating the patentability of the present claims. Early and favorable action of the merits of the present application is thereby respectfully requested.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Kristi L. Rupert, Ph.D. (Reg. No. 45,702) at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

Pursuant to 37 C.F.R. §§ 1.17 and 1.136(a), Applicant(s) respectfully petition(s) for a one (1) month extension of time for filing a reply in connection with the present application, and the required fee of \$120.00 is attached hereto.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or

credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

BIRCH, STEWART, KOLASCH & BIRCH, LLP

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GMM/KLR

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Attachments: Deposit receipts


BUDAPEST TREATY ON THE INTERNATIONAL  
RECOGNITION OF THE DEPOSIT OF MICROORGANISMS  
FOR THE PURPOSES OF PATENT PROCEDURE

INTERNATIONAL FORM

VTT Biotechnology and  
Food Research  
P.O. Box 1500

FIN-02044 VTT

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT  
issued pursuant to Rule 7.1 by the  
INTERNATIONAL DEPOSITARY AUTHORITY  
identified at the bottom of this page

<b>I. IDENTIFICATION OF THE MICROORGANISM</b>	
Identification reference given by the DEPOSITOR: VTT E-991203	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY: DSM 12728
<b>II. SCIENTIFIC DESCRIPTION AND/OR PROPOSED TAXONOMIC DESIGNATION</b>	
The microorganism identified under I. above was accompanied by:  (X ) a scientific description (X ) a proposed taxonomic designation  (Mark with a cross where applicable).	
<b>III. RECEIPT AND ACCEPTANCE</b>	
This International Depositary Authority accepts the microorganism identified under I. above, which was received by it on 1999-03-11 (Date of the original deposit) <sup>1</sup> .	
<b>IV. RECEIPT OF REQUEST FOR CONVERSION</b>	
The microorganism identified under I above was received by this International Depositary Authority on (date of original deposit) and a request to convert the original deposit to a deposit under the Budapest Treaty was received by it on (date of receipt of request for conversion).	
<b>V. INTERNATIONAL DEPOSITARY AUTHORITY</b>	
Name: DSMZ-DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH  Address: Mascheroder Weg 1b D-38124 Braunschweig	Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s):   Date: 1999-03-17

<sup>1</sup> Where Rule 6.4 (d) applies, such date is the date on which the status of international depositary authority was acquired.

BUDAPEST TREATY ON THE INTERNATIONAL  
RECOGNITION OF THE DEPOSIT OF MICROORGANISMS  
FOR THE PURPOSES OF PATENT PROCEDURE


INTERNATIONAL FORM

VTT Biotechnology and  
Food Research  
P.O.Box 1500

FIN-02044 VTT

VIABILITY STATEMENT

issued pursuant to Rule 10.2 by the  
INTERNATIONAL DEPOSITARY AUTHORITY  
identified at the bottom of this page

I. DEPOSITOR	II. IDENTIFICATION OF THE MICROORGANISM
<p>Name: VTT Biotechnology and Food Research Address: P.O.Box 1500  FIN-02044 VTT</p>	<p>Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY: DSM 12728  Date of the deposit or the transfer<sup>1</sup>: 1999-03-11</p>
III. VIABILITY STATEMENT	
<p>The viability of the microorganism identified under II above was tested on 1999-03-11<sup>2</sup>. On that date, the said microorganism was</p> <p>(X)<sup>3</sup> viable ( )<sup>3</sup> no longer viable</p>	
IV. CONDITIONS UNDER WHICH THE VIABILITY TEST HAS BEEN PERFORMED <sup>4</sup>	
V. INTERNATIONAL DEPOSITARY AUTHORITY	
<p>Name: DSMZ-DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH  Address: Mascheroder Weg 1b D-38124 Braunschweig</p>	<p>Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s):    Date: 1999-03-17</p>

- <sup>1</sup> Indicate the date of original deposit or, where a new deposit or a transfer has been made, the most recent relevant date (date of the new deposit or date of the transfer).  
<sup>2</sup> In the cases referred to in Rule 10.2(a) (ii) and (iii), refer to the most recent viability test.  
<sup>3</sup> Mark with a cross the applicable box.  
<sup>4</sup> Fill in if the information has been requested and if the results of the test were negative.


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INTERNATIONAL DEPOSITARY AUTHORITY  
identified at the bottom of this page

I. IDENTIFICATION OF THE MICROORGANISM	
Identification reference given by the DEPOSITOR: VTT E-991204	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY: DSM 12729
II. SCIENTIFIC DESCRIPTION AND/OR PROPOSED TAXONOMIC DESIGNATION	
<p>The microorganism identified under I. above was accompanied by:</p> <p>(X ) a scientific description (X ) a proposed taxonomic designation</p> <p>(Mark with a cross where applicable).</p>	
III. RECEIPT AND ACCEPTANCE	
<p>This International Depositary Authority accepts the microorganism identified under I. above, which was received by it on 1999-03-11 (Date of the original deposit)<sup>1</sup>.</p>	
IV. RECEIPT OF REQUEST FOR CONVERSION	
<p>The microorganism identified under I above was received by this International Depositary Authority on (date of original deposit) and a request to convert the original deposit to a deposit under the Budapest Treaty was received by it on (date of receipt of request for conversion).</p>	
V. INTERNATIONAL DEPOSITARY AUTHORITY	
Name: DSMZ-DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH  Address: Mascheroder Weg 1b D-38124 Braunschweig	Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s):   Date: 1999-03-17

<sup>1</sup> Where Rule 6.4 (d) applies, such date is the date on which the status of international depositary authority was acquired.

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Name: VTT Biotechnology and Food Research Address: P.O.Box 1500  FIN-02044 VTT	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY: DSM 12729  Date of the deposit or the transfer: 1999-03-11
III. VIABILITY STATEMENT	
The viability of the microorganism identified under II above was tested on 1999-03-11. On that date, the said microorganism was  (X) <sup>1</sup> viable  ( ) <sup>1</sup> no longer viable	
IV. CONDITIONS UNDER WHICH THE VIABILITY TEST HAS BEEN PERFORMED <sup>4</sup>	
V. INTERNATIONAL DEPOSITARY AUTHORITY	
Name: DSMZ-DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH  Address: Mascheroder Weg 1b D-38124 Braunschweig	Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s):    Date: 1999-03-17

- <sup>1</sup> Indicate the date of original deposit or, where a new deposit or a transfer has been made, the most recent relevant date (date of the new deposit or date of the transfer).
- <sup>2</sup> In the cases referred to in Rule 10.2(a) (ii) and (iii), refer to the most recent viability test.
- <sup>3</sup> Mark with a cross the applicable box.
- <sup>4</sup> Fill in if the information has been requested and if the results of the test were negative.